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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,628	12/19/2005	Abdullah Ibrahim Haj-Yehia	0-06-227/K8159/US/03	9260

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EXAMINER

CHU, YONG LIANG

ART UNIT	PAPER NUMBER
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1626

MAIL DATE	DELIVERY MODE
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07/23/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/536,628	Applicant(s) HAJ-YEHIA ET AL.	
	Examiner YONG CHU	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49-79 is/are pending in the application.
- 4a) Of the above claim(s) 49-71, 73-75 and 79 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 72 and 76-78 is/are rejected.
- 7) ☒ Claim(s) 72 and 76-78 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/23/2006 and 03/12/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 49-79 are pending in the instant application. Claims 49-71, 73-75 and 79 were withdrawn by the applicants as non-elected species due to restriction requirement. Claim 76 was mistakenly withdraw by applicant, and is rejoined to the other claims in Group IX.

Information Disclosure Statement

Applicants' Information Disclosure Statements, filed 03/23/2006 and 03/12/2007 have been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

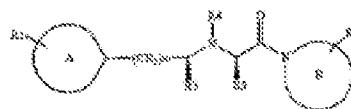
Priority

This application is a 371 of PCT/IL03/01006, filed on 11/27/2003, which claims benefit of U.S. Provisional Patent Applications 60/429,864, filed on 11/29/2002, and 60/430,003, filed on 11/29/2002.

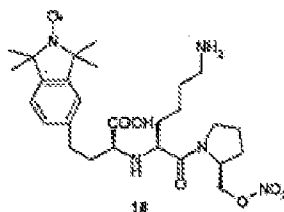
Response to Restriction

Applicants' election with traverse of Group IX (claims 72 and 76-78) drawn to a

multifunctional ACE-inhibitor compound of Formula (IV)



with

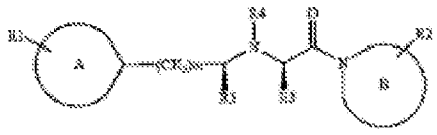


the elected species of compound 18 at page 65 of the specification in the reply filed on 03/03/2008 is acknowledged. Because the applicants do not make any argument regarding to the restriction requirement, it is regarded as election without traverse.

Status of the Claims

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:



An ACE-inhibitor compound of formula (IV)

wherein

ring **B** is optionally substituted saturated or unsaturated ring of from 4-7 carbon atoms;

R₂ is (CH₂)_n**X**, wherein **X** is –ONO₂; and the remaining substituents are as defined in claim 72.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter of claims 72 and 76-78 are further withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn compounds and compositions contain varying functional groups which are chemically recognized to differ in structure, function, and reactivity.

The scope of the invention is set in considering the elected species and the preferred embodiments. Therefore, claims 72 and 76-78 will be examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72 and 76-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The compounds in claim 72 has ring A and B, wherein one or both ring comprises said ROS (reactive oxygen species) scavenger component. The term "ROS scavenger" was defined at paragraph [0060] of the specification as superoxide dismutase (SOD) mimic, antioxidant and anti-inflammatory as examples. However, the specification does not describe what the other ROS scavengers are, what the ROS scavengers chemical structures are, and how these ROS scavengers are attached to the claimed ACE-inhibitor compounds.

Claim 78 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

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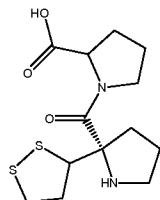
possession of the claimed invention. Claim 78 is rejected due to claiming “a second pharmaceutically active agent”. The specification does not describe what the second pharmaceutically active agent is, and how they can be formulated together with the instantly claimed ACE-inhibitor.

Claims 77-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 77-78 are rejected due to claiming a **“solvate”** of a compound of the Formula (IV) according to claim 72. The instant specification does not define a solvate. According to Vippagunta et al., *Advanced Drug Delivery Reviews*, page 1, a **solvate** exist as crystalline forms. They are specific crystalline forms of a compound that can crystallize in different forms, and not all compounds can form crystalline. The specification does not reasonably provide enablement for forming crystalline of each of the compound list in the claims. Because of high level of unpredictability associated with crystalline of the compounds, a greater amount of evidentiary support is needed to fully satisfy the requirement of 35 U.S.C 112, first paragraph. It is noted that crystallization art is unpredictable, requiring each embodiment to be individually assessed for the possibility. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will possess the crystalline form of the compound. To practice the

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claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compounds would form crystalline, with no assurance of success.

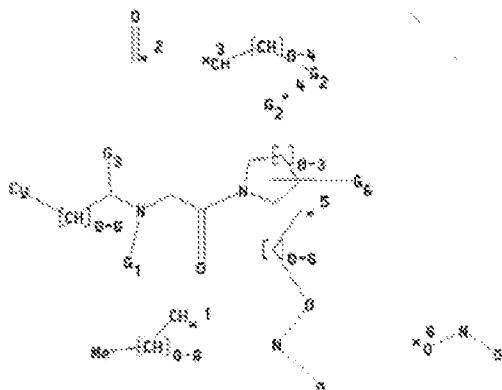
Claims 72 and 76-78 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Specifically, claims 72 and 76-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification although enabling for making compound 18, and the closely related compound wherein **ring A** is phenyl ring and **ring B** is pyrrolidin ring, does not enable one of ordinary skill in the art to make the vast number of other potential compounds, such as **ring B** is the other ring with 4 to 18 atoms. The instant specification also fails to describe how to use the claimed compound an ACE-inhibitor, even fails to describe how to use the elected species of compound 18 as ACE-inhibitor, because the specification does not show the elected species of compound has ACE inhibiting activity, or other activity. The specification discloses ACE activity of a single



compound *n-([2-((1,2)thiolan-3-yl)-prolinoyl]-pyrrolidine-2-carboxylic acid* in Example 9 at page 70 of the specification.

However, this compound does not even read into the examined scope of invention. A STN search of chemical compounds of related scope

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leads no prior art teaching of the compounds and

applications, see Cited-ref-STN serach-10536628. Pharmaceutical field is highly unpredictable. To be an ACE inhibitor, a compound has to bind to the ACE enzyme. The enzyme is highly spatial specific, and the compounds need to be tested and systemically screened toward each candidate compounds for their inhibiting activity, see *Camille Wermuth, Drug Discovery Today*, Vol. 11, 2006, p.348. Because of high level of unpredictability associated with the ACE-inhibitor, a greater amount of evidentiary support is needed to fully satisfy the requirement of 35 U.S.C 112, first paragraph. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that compounds fall within the scope of a claim will posses the crystalline form of the compound. To practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compounds would form crystalline, with no assurance of success.

Claim Objections

Claims 72 and 76-78 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Conclusion

- Claims 72 and 76-78 are objected to.
- Claims 72 and 76-78 are rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Status Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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